

REMARKS/ARGUMENTS

I. Status of Claims and Formal Matters

Claims 24-32, 43-53 and 64 were pending and under active consideration in this application at the time of the Office Action and stand rejected under 35 U.S.C. § 103(a). Applicants respectfully request reconsideration of the rejection in view of the current response.

II. Patentability Arguments

A. Claim Rejections

1) The Rejections under 35 U.S.C. 103(a) Should be Withdrawn

Claims 24-32, 43-53 and 64 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over by Cham *et al.* (Cancer Letters, 55 (1990) 221-225) (hereinafter “Cham”). Specifically, according to the Examiner, Cham discloses a composition comprising glycoalkaloids (BEC) useful for treating cancer (page 221) and further discloses that rhamnose inhibits the efficacy of BEC and that the aglycone solasodine is not effective against murine S180 (page 221). Applicants traverse the rejections in view of the following arguments.

Applicants agree with the Examiner’s assertion that Cham teaches that a composition comprising glycoalkaloids is useful for treating cancer. Applicants also agree that Cham discloses that the *exogenous addition* of rhamnose inhibits the efficacy of the composition. However, Applicants respectfully submit that the pending claims are not obvious over Cham because one of ordinary skill in the art would not have been motivated to remove rhamnose and aglycones from the BEC composition because Cham does not teach that rhamnose and aglycones are present in the BEC composition as degradation products.

First, Cham fails to disclose that rhamnose is a degradation product of solasonine and/or solamargine. The Examiner notes that Cham states “[r]hamnose is not found in mammalian glycoconjugates but forms part of solasonine, solamargine and diglycosides of solasodine found in BEC.” However, this portion of Cham simply does not constitute a teaching of the fact that either of the triglycoalkaloids of interest (or indeed the diglycoalkaloids/diglycosides present in the Cham composition) degrades to generate rhamnose **when forming part of the BEC composition**. BEC is isolated from a plant, not a mammal, so the fact that rhamnose is not found in mammalian glycoconjugates is inapposite. Cham teaches no more than the fact that

rhamnose is isolated from plant material with the solasonine and solamargine glycosides. The Examiner asserts that “since rhamnose is part of glycoalkaloids, upon their degradation,” rhamnose would be released. Applicants respectfully submit that the Examiner has inferred a teaching that is simply not present in Cham – that is, that the glycoalkaloids degrade **once they have been isolated from the plant material**. At its most generous interpretation, which Applicants in no way acknowledge is supportable, the reference by Cham to the existence of a rhamnose moiety in the glycoalkaloids of interest might be taken to imply that the rhamnose present in the isolated BEC is rhamnose derived from the glycoalkaloids either *in situ* in the extant plant or as part of the isolation process. Applicants submit that this cannot be understood by a person skilled in the art to constitute a teaching that rhamnose is produced by the degradation of glycoalkaloids in isolated glycoalkaloid compositions. Absent such a teaching, there can be no motivation to remove the degradation products.

Furthermore, with respect to the Examiner’s assertion that “it is generally acknowledged that it is desirable for the active component in a pharmaceutical composition to be as pure as possible,” such an assertion is subject to the proviso that the removal of any component of a pharmaceutical composition is a decision that involves a consideration of the relative detriment of the presence of the component and the costs associated with its removal. For example, if a component has a minor effect on the efficacy of the composition, yet its removal would significantly complicate the manufacturing process and thus significantly increase the cost of the drug, then it is not desirable to remove the component. As the Examiner has observed, the person skilled in the art is no position to know how much rhamnose is used in any of the BEC samples tested in Cham. Accordingly, the person skilled in the art cannot draw any quantitative relationship between the rhamnose content and the extent of inhibition of the activity of the composition. As discussed above, Cham reports rhamnose *exogenously added* to the composition but does not disclose that rhamnose is present as a degradation product. Accordingly, a person of ordinary skill in the art reading Cham, (1) is not taught that (intact)

rhamnose is present in the solution as a degradation product and (2) even were such person to improperly infer the presence of rhamnose as a degradation product of the glycoalkaloids (as opposed to rhamnose added or extracted with the glycoalkaloids), no conclusion can be drawn as to whether it would be present in an amount sufficient to warrant the cost associated with removal. Applicants have discovered that it is.

It is only with Applicant's discovery that isolated/purified glycoalkaloid compositions such as BEC (1) degrade to produce rhamnose (2) at levels that warrant its removal, that one of ordinary skill in the art is motivated to remove such degradation products, as presently claimed. The pending method claims require that the free sugars that are removed are the degradation products of glycoalkaloids present in a purified crystalline or semicrystalline glycoalkaloid preparation. The claims are not directed to the removal of rhamnose *per se*, but to rhamnose (and other free sugars) derived from the degradation of the glycoalkaloids in the purified crystalline or semicrystalline glycoalkaloid preparation. The removal of rhamnose that is isolated with the glycoalkaloids from plant material is not claimed.

In sum, it is clear that the presently claimed invention is nonobvious over Cham. Accordingly, Applicants respectfully request withdrawal of the rejections of claims 24-32, 43-53 and 64 under 35 U.S.C. § 103(a).

CONCLUSION.

Applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. The Examiner is hereby respectfully invited to contact the undersigned attorney at the telephone number listed below with any questions, comments, or suggestions relating to this application that may advance this application to allowance.

Respectfully submitted,

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